Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for constructing a variant set for modifying an antibody of interest, the method comprising:

(a) identifying a plurality of positions in said antibody of interest and, for each respective position in said plurality of positions, one or more substitutions for the respective position, wherein the plurality of positions and the one or more substitutions for each respective position in the plurality of positions collectively define an antibody sequence space;

(b) selecting a first plurality of variants of the antibody of interest, thereby forming a variant set, wherein said variant set comprises a subset of said antibody sequence space;

~~(c) measuring a property of all or a portion of the variants in said variant set;~~

~~(d)~~ (c) modeling ~~on~~ , using a suitably programmed computer, ~~a computer~~ a plurality of sequence-activity relationships, wherein

each respective sequence-activity relationship in said plurality of sequence-activity relationships is between (i) a respective plurality of descriptors, wherein each descriptor in the respective plurality of descriptors is a descriptor for one or more corresponding substitutions at one or more corresponding positions of the antibody of interest in the variant set and (ii) a plurality of quantitative measures of [[the]] a property, wherein each quantitative measure in the plurality of quantitative measures is a measurement of the property exhibited by ~~measured for each~~ a different variant in ~~all or said portion of the variants in~~ the variant set, and wherein

each respective sequence-activity relationship in said plurality of sequence-activity relationships includes at least one descriptor that is found in another sequence-activity relationship in said plurality of sequence-activity relationships;

each respective sequence-activity relationship in said plurality of sequence-activity relationships is either

(A) between (i) a subset of the plurality of descriptors and (ii) the plurality of quantitative measures or

(B) between (i) the plurality of descriptors and (ii) a subset of the plurality of quantitative measures;

each descriptor in the plurality of descriptors is weighted by a corresponding weight in a plurality of weights, and wherein said modeling comprises determining, for each respective weight in the plurality of weights, a respective first value and a respective second value for the respective weight using sequence-activity relationships in the plurality of sequence-activity relationships that include the descriptor corresponding to the weight, wherein the respective second value is a measure of confidence in the respective first value

~~, and then deriving from the sequence-activity relationship (A) a first value for a contribution to the measured property by the one or more substitutions at one or more positions in the plurality of positions in the antibody of interest, and (B) a second value quantifying a confidence with which the contribution to the measured property by the one or more substitutions at one or more positions of the antibody of interest can be assigned; and~~

~~(e) outputting said first value and said second value to a user, a display, or a tangible computer readable storage medium~~.

2. (Currently amended) The method of claim 1, the method further comprising repeating said (b) selecting~~, measuring (c),~~ and said modeling ~~(d)~~ (c) until a variant in said variant set exhibits a value for said property that exceeds a predetermined value.

3. (Original) The method of claim 2 wherein said predetermined value is a value that is greater than the value for the property that is exhibited by said antibody of interest.

4. (Withdrawn, Currently amended) The method of claim 1, the method further comprising repeating said (b) selecting~~, measuring (c),~~ and said modeling ~~(d)~~ (c) until a variant in said variant set exhibits a value for said property that is less than a predetermined value.

5. (Previously presented) The method of claim 1, wherein said plurality of positions and the one or more substitutions for each respective position in the plurality of positions are identified by said identifying (a) using a plurality of rules.

6. (Previously presented) The method of claim 5, wherein each rule in the plurality of rules defines an action to be taken in response to a computational test selected from the group of computational tests consisting of:

(i) a proximity of a position in the plurality of positions to a structurally defined region within the antibody;

(ii) a physico-chemical property of an amino acid at a position within a plurality of antibody sequences;

(iii) a principal component analysis of amino acids found at one or more positions within a plurality of antibody sequences;

(iv) a presence or an absence of a substitution in an antibody that is homologous to said antibody of interest;

(v) a presence or an absence of a substitution in a specific class of antibodies that are homologous to said antibody of interest;

(vi) a favorability of a substitution to a position in the antibody of interest calculated using a substitution matrix;

(vii) a probability of a substitution to a position in the antibody of interest calculated from a conservation index;

(viii) a favorability of a substitution to a position in the antibody of interest calculated from a comparison of homologous sequences;

(ix) a mutability of a position in the antibody of interest calculated from a comparison of homologous sequences;

(x) a favorability of a substitution to a position in the antibody of interest calculated from a comparison of structures that are homologous to said antibody of interest; and

(xi) a mutability of a position in the antibody of interest calculated from a comparison of structures that are homologous to said antibody of interest.

7. (Cancelled)

8. (Currently amended) The method of claim 1, wherein ~~said first value describes a relationship between the property measured by said measuring (c) and:~~ a descriptor in the plurality of descriptors is

(i) a substitution at a position in said plurality of positions represented by all or ~~said~~ a portion of the variants in said variant set,

(ii) a plurality of substitutions at a position in said plurality of positions represented by all or ~~said~~ a portion of the variants in said variant set, or

(iii) one or more substitutions in one or more positions in said plurality of positions represented by all or ~~said~~ a portion of the variants in said variant set.

9. (Currently amended) The method of claim 8, wherein a sequence-activity relationship in said plurality of sequence relationships is modeled by said modeling (c) by a method that comprises regressing:

$$V_{measured} = W_{11}P_1S_1 + W_{12}P_1S_2 + \ldots + W_{1N}P_1S_N + \ldots + W_{M1}P_MS_1 + W_{M2}P_MS_2 + \ldots + W_{MN}P_MS_N$$

wherein,

$V_{measured}$ is the measured property exhibited by ~~measured in all or said portion of the~~ variants in said variant set by said measuring (c);

W_{MN} is a contribution to [[a]] the measured property by one or more substitutions at one or more positions in the plurality of positions of the antibody of interest;

P_M is a position in said plurality of positions in said antibody of interest; and

S_N is a substitution at a position in the plurality of positions in said antibody of interest.

10. (Original) The method of claim 9, wherein said regressing comprises linear regression, non-linear regression, logistic regression, multivariate data analysis, or partial least squares projection to latent variables.

11. (Currently amended) The method of claim 1, wherein the modeling of a sequence-activity relationship in said plurality of sequence activity relationships in said modeling ~~(d)~~ (c) comprises computation of a neural network, computation of a Bayesian model, computation of a generalized additive model, computation of a support vector machine, or classification using a regression tree.

12. (Withdrawn, Currently amended) The method of claim 1, wherein said modeling ~~(d)~~ (c) comprises boosting or adaptive boosting.

13. (Currently amended) The method of claim 1, the method further comprising redefining said variant set to comprise variants in said antibody sequence space that include substitutions

in said plurality of positions that are selected based on a function of said respective first ~~value~~ values and said respective second ~~value~~ values by:

computing a modified respective first value by modifying the respective first value based on a function of the corresponding respective second value; and

computing a predicted score, for each respective variant in a population of variants of said antibody of interest, using the modified first value wherein each variant in said population of variants includes a substitution at one or more positions in said plurality of positions in said antibody of interest; and

redefining said variant set by selecting variants from among said population of variants as a function of the predicted score received by each variant in said set of variants.

14. (Currently amended) The method of claim 13, the method further comprising:

ranking said population of variants, wherein each variant in said population of variants is ranked based on the predicted score received by the variant based upon ~~the~~ a sequence-activity relationship in the plurality of sequence-activity relationships or a combination of sequence-activity relationship in the plurality of sequence-activity relationships; and

said selecting comprising accepting a predetermined percentage of the top ranked variants in said population of variants for said variant set.

15. (Cancelled)

16. (Withdrawn) The method of claim 13, wherein said redefining comprises redefining said variant set to comprise one or more variants of the antibody that are not in the antibody sequence space of said identifying (a).

17-19. (Cancelled)

20. (Withdrawn) The method of claim 13, wherein said redefining further comprises redefining said variant set to comprise one or more variants each having a substitution in a position in said plurality of positions not present in any variant in the variant set selected by said selecting (b).

21. (Withdrawn, Currently amended) The method of claim 5, wherein the contribution of each respective rule in said plurality of rules to the defining of said antibody sequence space is independently weighted by a rule weight in a plurality of rule weights corresponding to the respective rule, the method further comprising:

adjusting one or more rule weights in said plurality of rule weights based on a comparison, for each respective substitution at each position in the plurality of positions in the variant set, of (i) a value derived for the respective substitution from ~~the~~ a sequence-activity relationship in the plurality of sequence-activity relationships or a combination of sequence activity relationships in the plurality of sequence-activity relationships, and (ii) a score assigned by the plurality of rules to the respective substitution;

repeating said identifying step using said rule weights, thereby redefining said plurality of positions and, for each respective position in said plurality of positions, redefining the one or more substitutions for the respective position; and

redefining said variant set to comprise one or more variants that are not in the subset of the antibody sequence space formed in said selecting (b).

22-48. (Cancelled)

49. (Withdrawn, Currently amended) The method of claim 1 wherein

~~said measuring (c) comprises synthesizing all or~~ said ~~portion of the variants in~~ said ~~variant set, and wherein~~

said property of a variant in said variant set is a level of expression of said variant in a host cell, a susceptibility of said variant to a post-translational modification, a killing of a pathogenic organism or a virus resulting from an activity of said variant, a modulation of a signaling pathway by said variant, a modulation of surface density of a cell-surface receptor by said variant, a binding of a cellular growth factor receptor by said variant, a binding of a receptor or a mediator of tumor-driven angiogenesis by said variant, a binding of a B cell surface antigen by said variant, a binding of a protein synthesized by said variant, an induction of an antibody-mediated cell killing by said variant, an induction of an antibody-dependent macrophage activity by said variant, an induction of a histamine release by said variant, an induction of or cross-reaction with an anti-idiotype antibody by said variant, an immunogenicity of said variant, a reduction of viral titer by said variant or an immunomodulatory activity of said variant.

50. (Currently amended) The method of claim 1, wherein a said sequence-activity relationship in said plurality of sequence relationships has the form:

$$Y = f(w_1x_1, w_2x_2,\ldots, w_ix_i)$$

wherein,

Y is a quantitative measure of said property in said plurality of quantitative measures;

x_i is a descriptor, in the plurality of descriptors, of a substitution, a combination of substitutions, or a component of one or more substitutions, at one or more positions in said plurality of positions;

w_i is a weight applied to descriptor x_i; and

f( ) is a mathematical function.

51. (Currently amended) The method of claim 50, wherein said modeling of a sequence-activity relationship in a plurality of sequence activity relationships comprises regressing:

$$Y = f(w_1x_1, w_2x_2,\ldots, w_ix_i).$$

52. (Previously presented) The method of claim 51, wherein regressing comprises linear regression, non-linear regression, logistic regressing, or partial least squares projection to latent variables.

53-73. (Cancelled)

74. (Previously presented) The method of claim 1 wherein said antibody of interest is from rat, mouse, chicken, cow, monkey, pig, dog, rabbit, or human.

75. (Original) The method of claim 1 wherein said antibody of interest is a monoclonal antibody, a bispecific antibody, a multispecific antibody, a humanized antibody, a chimeric antibody, a camelised antibody, a single domain antibody, a single-chain Fvs (ScFv), a single chain antibody, a Fab fragment, a F(ab') fragment, a disulfide-linked Fvs (sdFv), or an anti-idiotypic (anti-Id) antibody.

76. (Original) The method of claim 1 wherein said antibody of interest is an epitope-binding fragment of a monoclonal antibody, an epitope-binding fragment of a bispecific antibody, an epitope-binding fragment of a multispecific antibody, an epitope-binding fragment of a humanized antibody, an epitope-binding fragment of a chimeric antibody, an epitope-binding fragment of a camelised antibody, an epitope-binding fragment of a single domain antibody, an epitope-binding fragment of a single-chain Fvs (ScFv), an epitope-binding fragment of a single chain antibody, an epitope-binding fragment of a Fab fragment, an epitope-binding fragment of a F(ab') fragment, an epitope-binding fragment of a disulfide-linke Fvs (sdFv), or an epitope-binding fragment of an anti-idiotypic (anti-Id) antibody.

77. (Original) The method of claim 1 wherein said antibody of interest is an antibody fragment.

78. (Original) The method of claim 1 wherein a variant in the variant set comprises a monoclonal antibody, a bispecific antibody, a multispecific antibody, a humanized antibody, a chimeric antibody, a camelised antibody, a single domain antibody, a single-chain Fvs (ScFv), a single chain antibody, a Fab fragment, a F(ab') fragment, a disulfide-linked Fvs (sdFv), or an anti-idiotypic (anti-Id) antibody.

79. (Original) The method of claim 1 wherein a variant in the variant set comprises an epitope-binding fragment of a monoclonal antibody, an epitope-binding fragment of a bispecific antibody, an epitope-binding fragment of a multispecific antibody, an epitope-binding fragment of a humanized antibody, an epitope-binding fragment of a chimeric antibody, an epitope-binding fragment of a camelised antibody, an epitope-binding fragment of a single domain antibody, an epitope-binding fragment of a single-chain Fvs (ScFv), an epitope-binding fragment of a single chain antibody, an epitope-binding fragment of a Fab fragment, an epitope-binding fragment of a F(ab') fragment, an epitope-binding fragment of a disulfide-linke Fvs (sdFv), or an epitope-binding fragment of an anti-idiotypic (anti-Id) antibody.

80. (Original) The method of claim 1 wherein a variant in said variant set comprises an antibody fragment.

81. (Withdrawn, Currently amended) The method of claim 1 wherein ~~said measuring said property of all or said portion of the variants in the measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by:

expressing a variant in the variant set in a cell line; and

measuring a cell-surface receptor surface density of said cell line that includes said variant.

82. (Withdrawn, Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by:

expressing a variant in the variant set in a cell line; and

measuring a cell surface receptor internalization rate of said cell line that includes said variant.

83. (Withdrawn, Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by:

expressing a variant in the variant set in a cell line; and

measuring a cell surface receptor post-translational modification of said cell line that includes said variant.

84. (Original) The method of claim 83 wherein said cell surface receptor post-translational modification is phosphorylation.

85. (Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by:

expressing a variant in the variant set in a cell line; and

measuring a binding of an antigen to said cell line that includes said variant.

86. (Original) The method of claim 85 wherein said antigen is a cellular growth factor receptor, a receptor of tumor-driven angiogenesis, a mediator of tumor-driven angiogenesis, a B cell surface antigen, or a protein synthesized by or in response to a pathogen.

87. (Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by measuring the ability for a variant in said variant set to immunospecifically bind to an antigen.

88. (Original) The method of claim 87 wherein said measuring comprises placing said variant in solution, spotting said variant onto a microchip, placing a polynucleotide encoding said variant in bacteria, placing a polynucleotide that codes for said variant in a spore, placing a polynucleotide that codes for said variant in a plasmid, or placing a polynucleotide that codes for said variant in phage.

89. (Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by assaying for a reduction of a viral titer of a virus in infected tissue culture cells by a variant in all or said portion of the variant set.

90. (Previously presented) The method of claim 89, wherein the virus is hepatitis A virus, hepatitis B virus, hepatitis C virus, human papilloma virus, human immunodeficiency virus, respiratory syncitial virus, human adenovirus, fowl adenovirus 1, African swine fever virus, lymphocytic choriomeningitis virus, ippy virus, lassa virus, equine arteritis virus, human astrovirus 1, autographa californica nucleopolyhedrovirus, plodia interpunctella granulovirus, commelina yellow mottle virus, rice tungro bacilliform virus, mushroom bacilliform virus, infectious pancreatic necrosis virus, infectious bursal disease virus, drosophila x virus, alfalfa mosaic virus, tobacco streak virus, brome mosaic virus, cucumber mosaic virus, apple stem grooving virus, carnation latent virus, cauliflower mosaic virus, chicken anemia virus, beet yellows virus, cowpea mosaic virus, tobacco ringspot virus, avian infectious bronchitis virus, alteromonas phage pm2, pseudomonas phage phi6, hepatitis delta virus, carnation ringspot virus, red clover necrotic mosaic virus, sweet clover necrotic mosaic virus, pea enation mosaic virus, ebola virus zair, soil-borne wheat mosaic virus, beet necrotic yellow vein virus, sulfobolus virus 1, maize streak virus, beet curly top virus, bean golden mosaic virus , duck hepatitis B virus, human herpesvirus, human herpesvirus, ateline herpesvirus 2, barley stripe mosaic virus, cryphonectria hypovirus 1-ep713,raspberry bushy dwarf virus, acholeplasma phage l51, chilo iridescent virus, goldfish virus 1, enterobacteria phage ms2, enterobacteria phage qbeta, thermoproteus virus 1, maize chlorotic mottle virus, maize rayado fino virus,

coliphage phix174, spiromicrovirus, spiroplasma phage, bdellomicrovirus, bdellovibrio phage, chlamydiamicrovirus, chlamydia phage 1, coliphage t4, tobacco necrosis virus, nodamura virus, influenzavirus a, influenzavirus C, thogoto virus, rabbit (shope) papillomavirus, human parainfluenza virus, measles virus, rubulavirus, mumps virus, human respiratory syncytial virus, gaeumannomyces graminis virus, penicillium chrysogenum virus, white clover cryptic virus, white clover cryptic virus 2, minute mice virus, adeno-associated virus, junonia coenia densovirus, bombyx mori virus, aedes aegypti densovirus, 1-paramecium bursaria chlorella nc64a virus, paramecium bursaria chlorella virus, 2-paramecium bursaria chlorella pbi virus, 3-hydra viridis chlorella virus, human poliovirus 1, human rhinovirus 1A, hepatovirus, encephalomyocarditis virus, foot-and-mouth disease virus, acholeplasma phage l2, coliphage t7, campoletis sonorensis virus, cotesia melanoscela virus, potato virus X, potato virus Y, ryegrass mosaic virus, barley yellow mosaic virus, fowlpox virus, sheep pox virus, swinepox virus, molluscum contagiosum virus, yaba monkey tumor virus, entomopoxvirus A, melolontha melolontha entomopoxvirus, amsacta moorei entomopoxvirus, chironomus luridus entomopoxvirus, reovirus 3, epizootic hemarrhogic disease virus 1, or simian rotavirus SA11.

91. (Withdrawn, Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by assaying for a reduction of a viral titer of a virus in an animal model by a variant in all or said portion of the variant set.

92. (Withdrawn) The method of claim 91 wherein the virus is hepatitis A virus, hepatitis B virus, hepatitis C virus, human papilloma virus, human immunodeficiency virus, respiratory syncitial virus, human adenovirus, fowl adenovirus 1, African swine fever virus, lymphocytic choriomeningitis virus, ippy virus, lassa virus, equine arteritis virus, human astrovirus 1, autographa californica nucleopolyhedrovirus, plodia interpunctella granulovirus, commelina yellow mottle virus, rice tungro bacilliform virus, mushroom bacilliform virus, infectious pancreatic necrosis virus, infectious bursal disease virus, drosophila x virus, alfalfa mosaic virus, tobacco streak virus, brome mosaic virus, cucumber mosaic virus, apple stem grooving virus, carnation latent virus, cauliflower mosaic virus, chicken anemia virus, beet yellows virus, cowpea mosaic virus, tobacco ringspot virus, avian infectious bronchitis virus, alteromonas phage pm2, pseudomonas phage phi6, hepatitis delta virus, carnation ringspot virus, red clover necrotic mosaic virus, sweet clover necrotic mosaic virus, pea enation mosaic virus, ebola virus

zair, soil-borne wheat mosaic virus, beet necrotic yellow vein virus, sulfobolus virus 1, maize streak virus, beet curly top virus, bean golden mosaic virus , duck hepatitis B virus, human herpesvirus, human herpesvirus, ateline herpesvirus 2, barley stripe mosaic virus, cryphonectria hypovirus 1-ep713,raspberry bushy dwarf virus, acholeplasma phage l51, chilo iridescent virus, goldfish virus 1, enterobacteria phage ms2, enterobacteria phage qbeta, thermoproteus virus 1, maize chlorotic mottle virus, maize rayado fino virus, coliphage phix174, spiromicrovirus, spiroplasma phage, bdellomicrovirus, bdellovibrio phage, chlamydiamicrovirus, chlamydia phage 1, coliphage t4, tobacco necrosis virus, nodamura virus, influenzavirus a, influenzavirus C, thogoto virus, rabbit (shope) papillomavirus, human parainfluenza virus, measles virus, rubulavirus, mumps virus, human respiratory syncytial virus, gaeumannomyces graminis virus, penicillium chrysogenum virus, white clover cryptic virus, white clover cryptic virus 2, minute mice virus, adeno-associated virus, junonia coenia densovirus, bombyx mori virus, aedes aegypti densovirus, 1-paramecium bursaria chlorella nc64a virus, paramecium bursaria chlorella virus, 2-paramecium bursaria chlorella pbi virus, 3-hydra viridis chlorella virus, human poliovirus 1, human rhinovirus 1A, hepatovirus, encephalomyocarditis virus, foot-and-mouth disease virus, acholeplasma phage l2, coliphage t7, campoletis sonorensis virus, cotesia melanoscela virus, potato virus X, potato virus Y, ryegrass mosaic virus, barley yellow mosaic virus, fowlpox virus, sheep pox virus, swinepox virus, molluscum contagiosum virus, yaba monkey tumor virus, entomopoxvirus A, melolontha melolontha entomopoxvirus, amsacta moorei entomopoxvirus, chironomus luridus entomopoxvirus, reovirus 3, epizootic hemarrhogic disease virus 1, or simian rotavirus SA11.

93. (Withdrawn, Currently amended) The method of claim 1 wherein ~~said measuring said property (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by assaying for a change in rate of proliferation of cells grown in a culture by a variant in all or said portion of the variant set.

94. (Withdrawn) The method of 93 wherein the cells grown in the culture are tumor cells, a cell line derived from tumor cells, a cell line derived from breast cancer cells, a cell line derived from ovarian cancer cells, a cell line derived from lung cancer cells, a cell line derived from bone cancer cells, a cell line derived from fibroblast cancer cells, a cell line derived from hematopoetic cancer cells, a cell line derived from testicular cancer cells, a cell line derived

from colon cancer cells, a cell line derived from prostate cancer cells, or a cell line derived from leukemia cells.

95. (Currently amended) The method of claim 1 wherein ~~said measuring (c) comprises~~ a quantitative measure in said plurality of quantitative measures is measured by assaying for a change in rate of proliferation of a specific cell type in an animal model by a variant in all or said portion of the redefined variant set.

96. (Original) The method of 95 wherein the specific cell type is a tumor cell type.

97. (Previously presented) The method of claim 95 wherein the specific cell type is derived from a breast cancer tumor, an ovarian cancer tumor, a lung cancer tumor, a bone cancer tumor, a fibroblast cancer, a hematopoetic cancer, a testicular cancer, a colon cancer, a prostate cancer, or a leukemia.

98-121. (Cancelled)

122. (Currently amended) The method of claim 13, wherein each variant in the redefined variant set differs by fewer than 5 substitutions from at least one variant for which the property has been measured ~~in said measuring (c)~~.

123. (Cancelled)

124. (Currently amended) The method of claim 5, wherein

the contribution of each respective rule in the plurality of rules to the defining of said antibody sequence space is independently weighted by a rule weight in a plurality of rule weights corresponding to the respective rule; and

the plurality of rule weights are calculated based on a comparison, for a plurality of substitutions in the variant set of (i) a value assigned to the respective substitution by a ~~the~~ sequence-activity relationship in the plurality of sequence-activity relationships or a combination of sequence-activity relationships in the plurality of sequence-activity relationships, and (ii) a score assigned by the plurality of rules to the respective substitution.

125. (Currently amended) The method of claim 1, wherein said modeling ~~(d)~~ (c) comprises deriving a relationship between (i) a physico-chemical property of one or more substitutions at one or more positions of the antibody of interest represented by the variant set and (ii) the property measured for all or the portion of the variants in the variant set.

126-127. (Cancelled)

128. (New) The method of claim 1, wherein the respective first value is an average of the respective weight from each sequence-activity relationship in the plurality of sequence-activity relationships that includes the respective weight.

129. (New) The method of claim 1, wherein the respective second value for a first weight in the plurality of weights is a standard deviation of the respective weight from each sequence-activity relationship in the plurality of sequence-activity relationships that includes the respective weight.

130. (New) The method of claim 1, the method further comprising:

(d) selecting a second plurality of variants of the antibody of interest, wherein each variant in said second plurality of variants has one or more substitutions, wherein a substitution in the one or more substitutions is characterized by a descriptor in the plurality of descriptors having a weight for which the modeling (c) determined a first value and a second value, wherein

the first value exceeds the second value,

the first value is an average or mean of the weight from each sequence-activity relationship in the plurality of sequence-activity relationships that includes the weight.

131. (New) The method of claim 130, wherein the second value is a standard deviation and the first value exceeds the second value by at least the standard deviation.

132. (New) The method of claim 130, wherein the second value is a standard deviation and the first value exceeds the second value by at least twice the standard deviation.

133. (New) The method of claim 130, wherein the second value is a standard deviation and the first value exceeds the second value by at least three times the standard deviation.

134. (New) The method of claim 1, wherein the respective second value for a first weight in the plurality of weights is a variance of the respective first value for the first weight.

135. (New) The method of claim 1, implemented on a computer.

136. (New) The method of claim 130, wherein a substitution in the one or more substitutions is found in at three variants in the variant set.

137. (New) The method of claim 130, wherein a first value for a descriptor is positive.

138. (New) The method of claim 1, wherein a respective first value is a mean of the corresponding weight from each sequence-activity relationship in the plurality of sequence-activity relationships that includes the respective weight.

139. (New) The method of claim 1, wherein a first value of a weight in the plurality of weights is a regression coefficient for the corresponding descriptor.

140. (New) The method of claim 1, wherein a first value of a weight in the plurality of weights for a sequence-activity relationship in the plurality of sequence-activity relationships is determined by a relative contribution of the corresponding descriptor in the plurality of descriptors to the property of the antibody in the sequence-activity relationship.

141. (New) The method of claim 1, wherein a first value of a weight in the plurality of weights for a sequence-activity relationship in the plurality of sequence-activity relationships is determined by an absolute contribution of the corresponding descriptor in the plurality of descriptors to the property of the antibody in the sequence-activity relationship.

142. (New) The method of claim 1, the method further comprising:

(d) using said modeling (c) to identify a variant of the antibody of interest that has a high probability of having an improved property relative to the antibody of interest.